Nové SSC guidelines 2016 cesta vpřed nebo krok zpět?

Vladimír Šrámek

ARK, FNUSA

Colors of Sepsis, 29.1.-2.2.2018

struktura přednášky

- rozdíly SSC guidelines 2016 – 2012 pro vybraná doporučení (iniciální resuscitace, ATB)
- nesouhlas s SCC guidelines (IDSA)
- SG sepse: Sepsis-3 a kontroverze

CONFERENCE REPORTS AND EXPERT PANEL

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

publikováno – leden 2017, 4. revize

doporučení SSC guidelines 2016

93 Recommendations

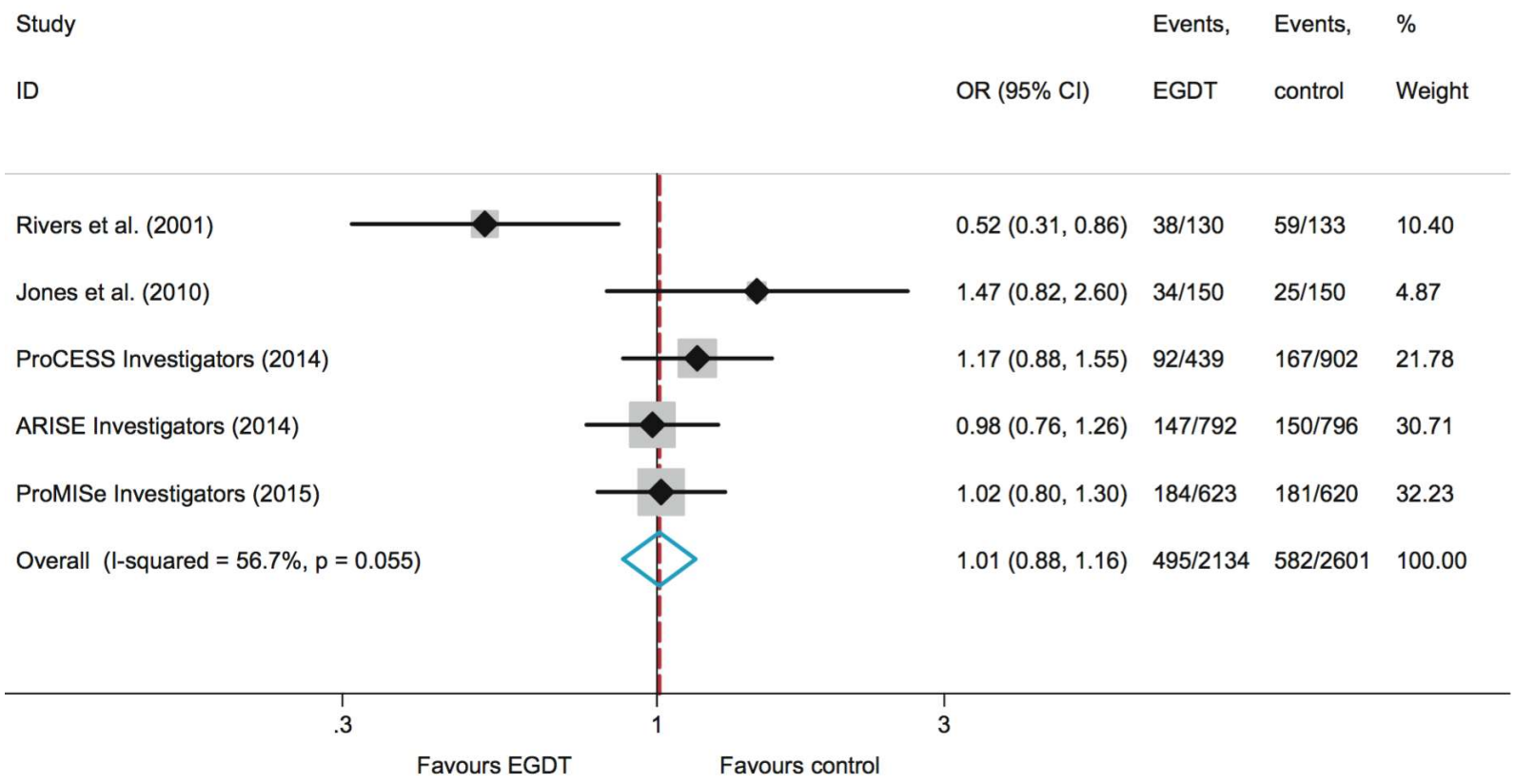
- 32 **Strong** recommendations: ***"We recommend"***
- 39 **Weak** recommendations: ***"We suggest"***
- 18 Best Practice Statements
- No recommendation provided for 4 PICO Que

Reagovala na „Sepsis Trilogy"

Reagovala na „Sepsis-3"

A systematic review and meta-analysis of early goal-directed therapy for septic shock: the ARISE, ProCESS and ProMISe Investigators

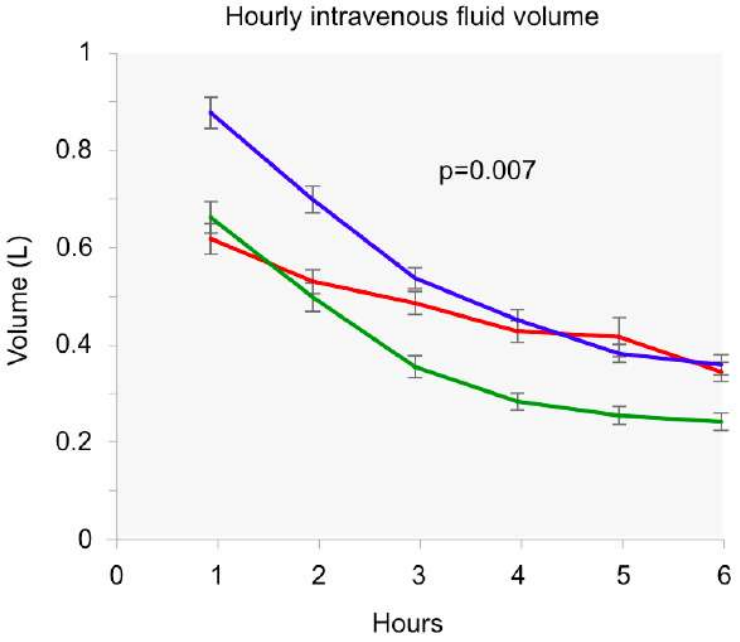
A Primary mortality outcome of each study

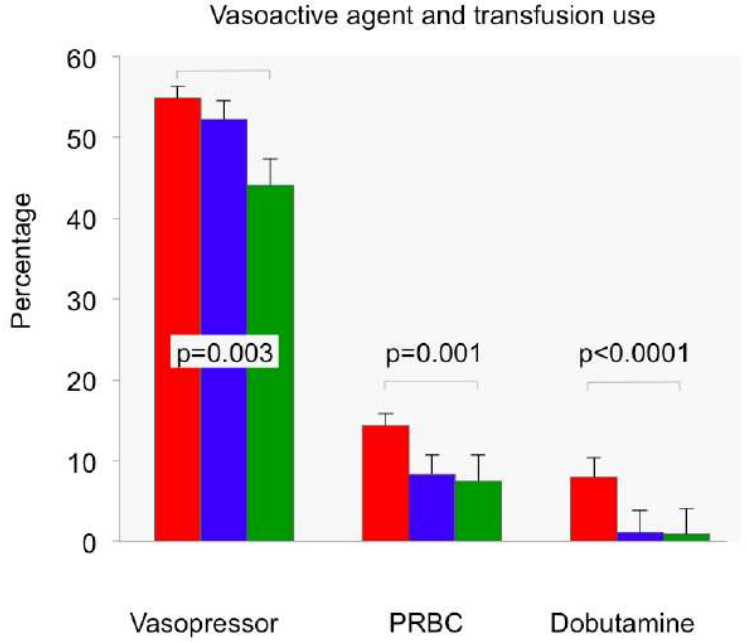


Intensive Care Med (2015) 41:1549–1560
DOI 10.1007/s00134-015-3822-1

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*





Protocol-based EGDT | Protocol-based Standard Therapy | Usual care

Intravenous Fluids		Intravenous Antibiotics	
EGDT	2.8 L	**EGDT**	97.5%
Usual Care	2.3 L	**Usual Care**	96.9%

DOI: 10.1056/NEJMoa1401602

„Sepsis Trilogy“ (ProCESS, ARISE, ProMISe)

- V roce 2014-5 byly publikovány tři multicentrické studie, provedené v US, Austrálii & Novém Zélandu a Anglii), které srovnávaly Riversův protokol se standardní péčí. Americká studie měla i třetí větev, definovanou jako neinvazivní, fyziologický protokol (charakteristika studií viz níže). Všechny studie ukázaly, že **standardní péče (definovaná jako časná identifikace problému, iniciální tekutinová resuscitace, zajištění perfuze tkání, včasné podání ATB a vedení léčby v prvních hodinách zkušeným lékařem) má stejné výsledky** jako složitější algoritmy.
- **ProCESS** (porovnání hospitalizační mortality v D60): n=1351 nemocných, 31 center, mortalita 21% (EGDT), 18,2% (modifikovaný protokol), 18,9% (standardní léčba)
- **ARISE** (porovnání „all cause“ mortality v D90): n=1600 nemocných, 51 center, mortalita 18,6% (EGDT) a 18,8% (standard).
- **ProMISe** (porovnání „all cause“ mortality v D90): n=1260 nemocných, 56 center, mortalita 29,5% (EGDT) a 29,2% (standard).
- Shrnující metaanalýza konstatuje, že EGDT není lepší než standardní péče o nemocné se septickým šokem v podmínkách emergency a je spojena se zvýšenou konzumací zdrojů (13).

2012 RECOMMENDATIONS

A. INITIAL RESUSCITATION

1. Protocolized, quantitave resuscitaon of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration 4 mmol/L). Goals during the first 6 hr resuscitation:

- a. Central venous pressure 8–12 mm Hg
- b. Mean arterial pressure ≥ 65 mm Hg
- c. Urine output ≥ 0.5 mL/kg/hr
- d. Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).

2. In patients with elevated lactate levels, targeting resuscitation to normalize lactate (grade 2C).

2016 RECOMMENDATIONS

A. INITIAL RESUSCITATION

1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).

2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, **at least 30 mL/kg of IV** crystalloid fluid be given within the first 3 hours (strong recommendaon, low quality of evidence).

3. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS).

Remarks: Reassessment should include a thorough clinical examinaon and evaluation of available physiologic variables (heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urine output, and others, as available) as well as other noninvasive or invasive monitoring,as available.

4. We recommend further hemodynamic assessment (such as assessing cardiac funcon) to determine the type of shock if the clinical examination does not lead to a clear diagnosis (BPS).

5. We suggest that dynamic over static variables be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence).

6. We recommend an initial target **MAP 65 mmHg** in patients with septic shock requiring vasopressors (strong recommendaon, moderate quality of evidence).

7. We suggest guiding **resuscitation to normalize lactate** in patients with elevated lactate levels as a marker of tissue hypoperfusion (weak recommendaon, low quality of evidence).

High versus Low Blood-Pressure Target in Patients with Septic Shock

We recommend an initial target mean arterial pressure of 65 mmHg in patients with septic shock requiring vasopressors.

(Strong recommendation; moderate quality of evidence)

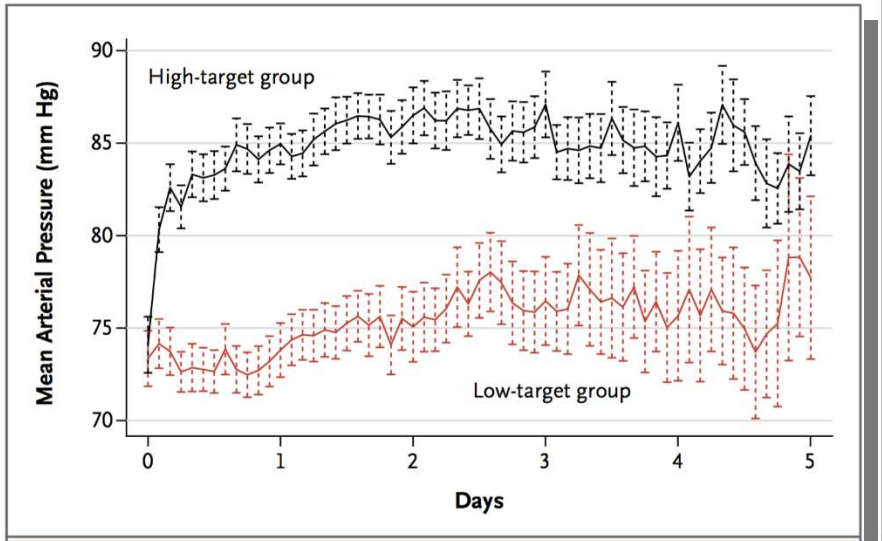


Figure 2. Mean Arterial Pressure during the 5-Day Study Period.

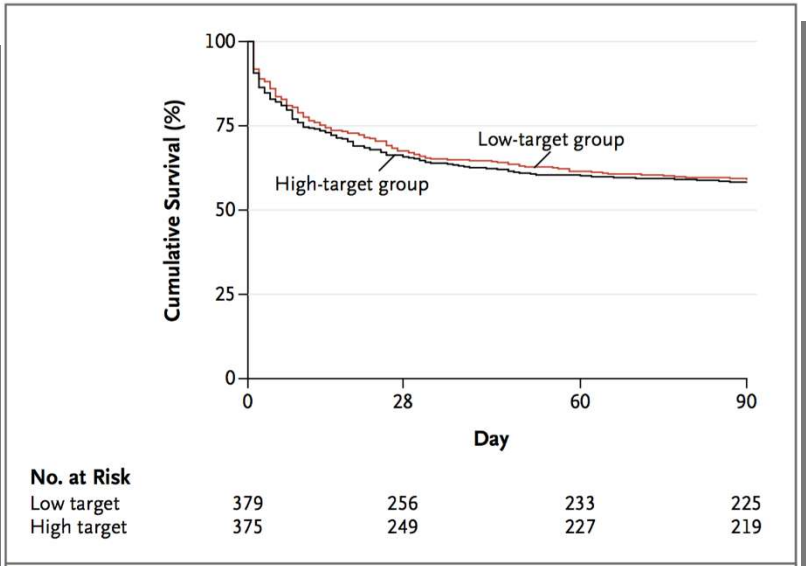


Figure 3. Kaplan–Meier Curves for Cumulative Survival.

DOI: 10.1056/NEJMoa1312173

Lactate can help guide resuscitation

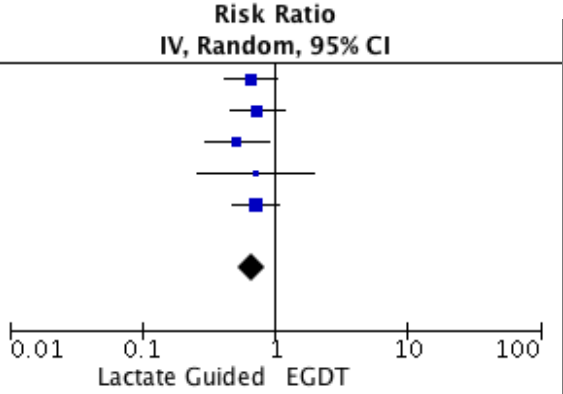
- **We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion.**

(Weak recommendation; low quality of evidence)

Study or Subgroup	Lactate Guided Events	Total	Standard Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Year
Jansen, 2010	20	68	30	67	24.9%	0.66 [0.42, 1.03]	2010
Jones, 2010	25	150	34	150	23.8%	0.74 [0.46, 1.17]	2010
Tian, 2012	14	43	12	19	16.9%	0.52 [0.30, 0.89]	2012
Yu, 2013	5	25	7	25	5.1%	0.71 [0.26, 1.95]	2013
Lyu 2015	20	50	28	50	29.2%	0.71 [0.47, 1.09]	2015
Total (95% CI)		**336**		**311**	**100.0%**	**0.67 [0.53, 0.84]**	
Total events	84		111				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.14$, df = 4 (P = 0.89); $I^2 = 0\%$

Test for overall effect: Z = 3.51 (P = 0.0004)



resuscitace hemodynamiky – jen tekutiny?

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

The NEW ENGLAND JOURNAL of MEDICINE

CONCLUSIONS

Fluid boluses significantly increased 48-hour mortality in critically ill children with impaired perfusion in these resource-limited settings in Africa. (Funded by the Medical Research Council, United Kingdom; FEAST Current Controlled Trials number, ISRCTN69856593.)

N ENGL J MED 364;26 NEJM.ORG JUNE 30, 2011

Maitland et al. BMC Medicine 2013, 11:68
http://www.biomedcentral.com/1741-7015/11/68

BMC Medicine

RESEARCH Open Access

Exploring mechanisms of excess mortality with early fluid resuscitation: insights from the FEAST trial

Kathryn Maitland[1,2*], Elizabeth C George[3], Jennifer A Evans[4], Sarah Kiguli[5], Peter Olupot-Olupot[6], Samuel O Akech[2],

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension A Randomized Clinical Trial

Ben Andrews, MD; Matthew W. Semler, MD, MSc; Lovy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chilesho Mabula, MBChB; Mwango Bwalya, MBChB; Gordon R. Bernard, MD

CONCLUSIONS AND RELEVANCE Among adults with sepsis and hypotension, most of whom were positive for HIV, in a resource-limited setting, a protocol for early resuscitation with administration of intravenous fluids and vasopressors increased in-hospital mortality compared with usual care. Further studies are needed to understand the effects of administration of intravenous fluid boluses and vasopressors in patients with sepsis across different low- and middle-income clinical settings and patient populations.

JAMA. 2017;318(13):1233-1240. doi:10.1001/jama.2017.10913

n=212

INITIAL RESUSCITATION - pokračování

ATB – 2kombinace na začátek SŠ, Pk/Pd

- **Combination therapy:** The use of multiple anbiotics (usually of different mechanistic classes) with the specific intent of covering the known or suspected pathogen(s) with more than one anbiotic (e.g., piperacillin/tazobactam and an aminoglycoside or fluoroquinolone for gram-negative pathogens) to accelerate pathogen clearance rather than to broaden antimicrobial coverage. Other proposed applications of combination therapy include inhibition of bacterial toxin production (e.g., clindamycin with B-lactams for streptococcal toxic shock) or potential immune modulatory effects (macrolides with a B-lactam for pneumococcal pneumonia).

Source control: vypadl 12 hod časový interval

Fluids: krystaloidy lepší než želatina, zůstal FR

Vasoaktivní látky: titrace vasopresinu, opatrně s dobutaminem

2012 RECOMMENDATIONS

C. DIAGNOSIS

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 min) in the start of antimicrobials (grade 1C).

2. Use of the 1,3-ß-D-glucan assay (grade 2B), mannan and an-mannan antibody assays (2C), if available,and invasive candidiasis in differential diagnosis of cause of infection.

3. Imaging studies performed promptly to confirm a potential source of infection (UG).

2016 RECOMMENDATIONS

C. DIAGNOSIS

1. We recommend that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis or septic shock if doing so results in no substantial delay in the start of antimicrobials (BPS).

Remarks: Appropriate routine microbiologic cultures always include at least two sets of blood cultures (aerobic and anaerobic).

Hemokultury
(aerobic + anaerobic)

SSC guidelines:

Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA (1983) The clinical
signifcance of positive blood cultures: a comprehensive analysis of
500 episodes of bacteremia and fungemia in adults. I. Laboratory and
epidemiologic observations. Rev Infect Dis 5(1):35–53

1. Chandler MT, Morton ES, Byrd RP Jr, et al. Reevaluation of anaerobic blood cultures in a Veteran population. South Med J 2000; 93:986–8.

2. Iwata K, Takahashi M. Is anaerobic blood culture necessary? If so, who needs it? Am J Med Sci 2008; 336:58–63.

3. Morris AJ, Wilson ML, Mirrett S, Reller LB. Rationale for selective use of anaerobic blood cultures. J Clin Microbiol 1993; 31:2110–3.

4. Salonen JH, Eerola E, Meurman O. Clinical significance and outcome of anaero-bic bacteremia. Clin Infect Dis 1998 ; 26:1413–7.

5. Ortiz E, Sande MA. Routine use of anaerobic blood cultures: are they still indi-cated? Am J Med 2000; 108:445–7.

6. Saito T, Senda K, Takakura S, et al. Anaerobic bacteremia: the yield of positive anaerobic blood cultures: patient characteristics and potential risk factors. Clin Chem Lab Med 2003; 41:293–7.

7. Grohs P, Mainardi JL, Podglajen I, et al. Relevance of routine use of the anaerobic blood culture bottle. J Clin Microbiol 2007 ; 45:2711–5.

8. Rosenblatt JE. Can we afford to do anaerobic cultures and identification? A positive point of view. Clin Infect Dis 1997; 25(Suppl 2):S127–31.

Clinical Infectious Diseases
VIEWPOINTS

Infectious Diseases Society of America (IDSA) POSITION STATEMENT: Why IDSA Did Not Endorse the Surviving Sepsis Campaign Guidelines

IDSA Sepsis Task Force*

- Suspected sepsis/septic shock
- ATB

Murri R, et al. IDSA Did Not Endorse the Surviving Sepsis Campaign Guidelines. Clin Infect Dis. 2017 Dec 20.

- BSI bez projevů sepse (podporující článek)

DG sepse (Sepsis-3)

Třetí konference, konaná pod záštitou SCCM/ESICM v roce 2015 navrhuje zásadní změny: opustit koncept SIRS a sepsi v podmínkách ICU definovat jako změnu orgánové funkce (definovanou jako dSOFA $\geq$ 2) způsobenou (suspektní) infekcí (1). Septický šok pak definovat jako hypotenzi vyžadující ke korekci (MAP > 65 mmHg) vazopresory a zároveň přítomnost tkáňové hypoperfúze (laktát > 2 mmol/l) (2).

1. Singer M, Deutschman CS, Seymour CW et al (2016) The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 315(8):801–810

2. Shankar-Hari M, Phillips GS, Levy ML et al (2016) Developing a new definition and assessing new clinical criteria for septic shock: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 315(8):775–787

3. Seymour CW, Liu VX, Iwashyna TJ et al (2016) Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for
Sepsis and Septic Shock (Sepsis-3). JAMA 315(8):762–774

DG sepse II

Konsensuální konference ACCP/SCCM, konaná v roce 1991, definovala sepsi jako aktivaci systémové zánětlivé odpovědi (SIRS) na přítomnost cizího (mikro)organizmu a stratifikovala její tíži (sepse, těžká sepse a septický šok).

Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest 1992 Jun;101(6):1644-55.

Konference konaná v roce 2001 upozornila na široké spektrum klinických i laboratorních známek sepse, doporučila pohlížet na proces šíření infekce jako na diseminaci rakoviny (PIRO koncept), základní stratifikaci sepse však nezměnila.

Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Intensive Care Med. 2003 Apr;29(4):530-8. Epub 2003 Mar 28.

spousta otázek

Some of the concerns raised …

- *‘SIRS is vital to diagnose sepsis and to treat patients early’*
- *‘SOFA won’t be measured daily on every patient’*
- *‘do I need to measure SOFA twice to measure change’*
- *‘lactate should be in the sepsis criteria’*
- *‘lactate should go from the septic shock criteria’*
- *’80% of the world cannot measure lactate’*
- *‘why not shock = hyperlactatemia OR hypotension?’*
- *‘patients will die if we wait until qSOFA hits ≥2 before treating’*
- *‘why don’t we just use qSOFA to diagnose sepsis?’*
- *‘the coders won’t like it’*
- *‘what about children?’ …*

ČR

DEFNICE SEPSE 2016 (SEPSIS-3)

Autoři: Sklienka P.[1,3], Beneš J.[2], Máca J.[1,3]

Článek: AIM, 27,2016, č.5, s.302-308

Dostál P: komentář výboru ČSIM v AIM
Šrámek V: Postgraduální medicína 5/2016

American Journal of Emergency Medicine 35 (2017) 1730–1733

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Brief Report

Comparison of QSOFA score and SIRS criteria as screening mechanisms for emergency department sepsis

Samir Haydar, DO, MPH, Matthew Spanier, MD *, Patricia Weems, MD, Samantha Wood, MD, Tania Strout, PhD, RN, MS

Maine Medical Center, Department of Emergency Medicine, Tufts University School of Medicine, 22 Bramhall Street, Portland, ME 04102, United States

ED, n=200
SAPCD

Conclusions: Although qSOFA may be valuable in predicting sepsis-related mortality, it performed poorly as a screening tool for identifying sepsis in the ED. As the time to meet qSOFA criteria was significantly longer than for SIRS, relying on qSOFA alone may delay initiation of evidence-based interventions known to improve sepsis-related outcomes.

ED, n=7754
SAPCD

An Emergency Department Validation of the SEP-3 Sepsis and Septic Shock Definitions and Comparison With 1992 Consensus Definitions

Daniel J. Henning, MD; Michael A. Puskarich, MD; Wesley H. Self, MD; Michael D. Howell, MD, MPH; Michael W. Donnino, MD; Donald M. Yealy, MD; Alan E. Jones, MD; Nathan I. Shapiro, MD, MPH*

Conclusion: Both the new SEP-3 and original sepsis definitions stratify ED patients at risk for mortality, albeit with differing performances. In terms of mortality prediction, the SEP-3 definitions had improved specificity, but at the cost of sensitivity. Use of either approach requires a clearly intended target: more sensitivity versus specificity. [Ann Emerg Med. 2017;70:544-552.]

Potential Impact of the 2016 Consensus Definitions of Sepsis and Septic Shock on Future Sepsis Research

Sandra L. Peake, FCICM, PhD*; Anthony Delaney, PhD, FACEM; Michael Bailey, MSc, PhD; Rinaldo Bellomo, MD, FCICM; for the ARISE Investigators†

Conclusion: Most ARISE participants did not meet the Sepsis-3 definition for septic shock at baseline. However, the majority fulfilled the new sepsis definition and mortality was higher than for participants not fulfilling the criteria. A quarter of participants meeting the new sepsis definition did not fulfill the qSOFA screening criteria, potentially limiting its utility as a screening tool for sepsis trials with patients with suspected infection in the ED. The implications of the new definitions for patients not eligible for recruitment into the ARISE trial are unknown. [Ann Emerg Med. 2017;70:553-561.]

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

A Systematic Review and Meta-Analysis

CHEST

Rodrigo Serafim, MD; Jose Andrade Gomes, MD; Jorge Salluh, MD, PhD; and Pedro Póvoa, MD, PhD

CONCLUSIONS: The SIRS was significantly superior to the qSOFA for sepsis diagnosis, and the qSOFA was slightly better than the SIRS in predicting hospital mortality. The association of both criteria could provide a better model to initiate or escalate therapy in patients with sepsis.

NRIP 2018 CZ

- **Povaha příjmu na JIP bude určena ve 4 krocích, které budou nově zadávány:**
- 1) operační/neoperační
- 2) urgentní/elektivní

- **3) sepse ANO/NE**

- 4) DG skupina dle orgánu/orgánového systému, který vedl k přijetí do intenzivní péče (IP)
-
- **Diagnostická skupina kód**
- Kardiovaskulární systém 1
- Stav po KPR 2
- CNS 3
- GIT 4
- Ledviny a urogenitální systém 5
- Trauma 6
- Respirační systém 7
- Metabolicko-endokrinní 8
- Ostatní 9
- Not applicable (NA) (např. příjem elektivní operace…) 10
-
- **B) orgánová dysfunkce**
-
- **SOFA při příjmu** (pro JIP vykazující TISS nad 30 bodů je povinná, pro ostatní alternativní)

2012 RECOMMENDATIONS

B. SCREENING FOR SEPSIS AND PERFORMANCE IMPROVEMENT

1. Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C).

2. Hospital-based performance improvement efforts in severe sepsis (UG).

2016 RECOMMENDATIONS

B. SCREENING FOR SEPSIS AND PERFORMANCE IMPROVEMENT

1. We recommend that hospitals and hospital systems have a performance improvement program for sepsis, including sepsis screening for acutely ill, highrisk patients (BPS).

Sepsis Performance Improvement

Snahy zlepšit „organizaci sepse“ v nemocničních zařízeních jsou spojeny s + dopadem na prognózu nemocných

Metaanalýza 50 observačních studií:

- Performance improvement programs associated with a significant increase in compliance with the SSC bundles and a reduction in mortality (OR 0.66; 95% CI 0.61-0.72).

- Damiani E, Donati A, Serafini G et al (2015) Effect of performance improvement programs on compliance with sepsis bundles and mortality: a systematic review and meta-analysis of observational studies. PLoS One 10(5):e0125827

Povinné hlášení: NYS, CMS, UK

závěr

Léčíme nemocného, kterého máme před očima

- nečekáme, až qSOFA≥2 nebo DSOFA ≥2
- léčíme infekci, oligurii, hypoxemii etc.

Diagnóza sepse: mozaika sepse

Terapie: (RIVERS)

- **Začni brzy (dej ATB)**
- **Koriguj hypovolémii**
- **Udržuj minimální perfúzní tlak**
- **… a někdy snad trochu něco navíc**